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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,743	12/20/2005	Efthimios Ippikoglou	02901/0203760-US0	8279
7278	7590	11/15/2006		
DARBY & DARBY P.C. P. O. BOX 5257 NEW YORK, NY 10150-5257				
			EXAMINER BASI, NIRMAL SINGH	
			ART UNIT 1646	PAPER NUMBER

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/561,743

Applicant(s)

IPPIKOLOU, EFTHIMIOS

Examiner

Nirmal S. Basi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30-37 is/are pending in the application.
- 4a) Of the above claim(s) 30-32 and 34-37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 October 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/20/05</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Amendments filed 12/20/05 and 7/24/06 have been entered.
2. CRF filed 4/13/06 has been entered.
3. Applicant's election with traverse of Group II (Claims 33) on 7/24/06 is acknowledged. The traversal is on the ground(s) that a search and examination of the entire application can be made without serious burden because the groups of claims are inter-related as they are directed to polynucleotides and polypeptides encoded by the same. Applicant's arguments have been fully considered but they are not found persuasive. A search of groups I-VI would not be co-extensive particularly with regard to the literature search or sequence search. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner. Accordingly, claims 30-32 and 34-37 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP 821.03.

The requirement is still deemed proper and is therefore made FINAL.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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5. Claim 33 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 33 recites a polypeptide but does not recite that it is isolated or purified. The claim as currently recited encompasses naturally-occurring compounds. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite an isolated and purified polypeptide to overcome this rejection.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lustbader (US Patent number 7,081,446) in view of Florkiewicz (Patent No. 5891855) and further in view of Boime et al. (Patent No. 6238890).

Claim 33 is drawn to a polypeptide (chimeric FSH molecule) comprising the amino acid sequence set forth in SEQ ID NO:27 (i.e. an alpha-FSH subunit and beta-FSH subunit construct).

Lustbader teaches a synthetic chimeric FSH construct comprising an alpha-FSH subunit and a beta-FSH subunit.

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Lustbader teaches the following embodiments:

- A. A synthetic FSH comprising a beta-FSH subunit, an alpha-FSH subunit and a half-life-increasing moiety, wherein the beta-FSH subunit, an alpha-FSH subunit and half-life-increasing moiety are covalently bound.
- B. A synthetic FSH comprising a beta FSH subunit, an alpha-FSH subunit and a polypeptide segment comprising the amino acid sequence ser-gly-ser-asn-ala-thr-gly-ser-gly-ser-asn-ala-thr-ser-gly-ser, (SEQ ID NO:9), wherein the beta-FSH subunit, an alpha-FSH subunit and polypeptide segment are covalently bound.
- C. The beta-FSH subunit, an alpha-FSH subunit are bound to each other via the half-life-increasing moiety, and in a preferred embodiment, the beta-FSH subunit, the alpha-FSH subunit and the polypeptide segment exist within a single polypeptide chain. In one embodiment, the beta-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, or conversely, the beta-FSH subunit is bound at its N-terminal end to the C-terminal end of the polypeptide segment.
- D. A synthetic FSH wherein the beta-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, and the polypeptide segment is bound at its C-terminal end to the N-terminal end of the alpha-FSH subunit.
- E. A synthetic FSH wherein the alpha-FSH subunit is bound at its C-terminal end to the N-terminal end of the polypeptide segment, and the polypeptide segment is bound at its C-terminal end to the N-terminal end of the beta-FSH

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subunit. In a further embodiment, the synthetic FSH comprises the N-terminal signal sequence of either the beta-FSH or alpha-FSH subunit. In an embodiment of any of the instant synthetic FSHs, the alpha-FSH subunit (if applicable) and beta-FSH subunit are from an animal selected from the group consisting of a primate, a horse, a sheep, a bird, a bovine, a pig, a dog, a cat, and a rodent. In the preferred embodiment, the alpha-FSH and/or beta-FSH subunit is a human subunit. In a further preferred embodiment, the alpha-FSH subunit (if applicable) and the beta-FSH subunit exist within a single polypeptide chain along with the half-life-increasing moiety.

G. A method for producing a synthetic FSH, which comprises co-expressing (i) a nucleic acid which encodes an alpha-FSH subunit, and (ii) a nucleic acid which encodes a polypeptide comprising a beta-FSH subunit and a polypeptide segment comprising the amino acid sequence ser-gly-ser-asn-ala-thr-gly-ser-gly-ser-asn-ala-thr-ser-gly-ser under conditions permitting such co-expression; and recovering the synthetic FSH so produced.

Lustbader does not disclose the synthetic chimeric polypeptide consisting of the alpha-FSH and beta-FSH disclosed in SEQ ID NO:27.

Florkiewicz (Patent No. 5891855) teaches the alpha-FSH subunit (SEQ ID NO:5) which is identical to amino acids 1-116 of SEQ ID NO:27 of instant application.

Query Match 50.5%; Score 643; DB 1; Length 116;  
Best Local Similarity 100.0%; Pred. No. 8.7e-53;  
Matches 116; Conservative 0; Mismatches 0; Indels 0;  
Gaps 0;

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Qy 1  
MDYYRKYAAIFLVTLFVFLHVLHSAPDVQDCPECTLQENPFFSQPGAPILQCMGCCFSRA 60

|||||  
Db 1  
MDYYRKYAAIFLVTLFVFLHVLHSAPDVQDCPECTLQENPFFSQPGAPILQCMGCCFSRA 60

Qy 61 YPTPLRSKKTMLVQKNVTSESTCCVAKSYNRVTVMGGFKVENHTACHCSTCYHKS  
116

|||||  
Db 61 YPTPLRSKKTMLVQKNVTSESTCCVAKSYNRVTVMGGFKVENHTACHCSTCYHKS  
116

Boime (Patent No. 6238890) teaches beta-FSH subunit (SEQ ID NO:12) which is identical to amino acids 117-227 of SEQ ID NO:27 of instant application.

Query Match 49.5%; Score 630; DB 2; Length 229;  
Best Local Similarity 100.0%; Pred. No. 3.2e-51;  
Matches 111; Conservative 0; Mismatches 0; Indels 0;  
Gaps 0;

Qy 117  
NSCELTNITIAIEKEECRFCISINTTWCAGYCYTRDLVYKDPARPKIQKTCTFKELVYET 176

|||||  
Db 19  
NSCELTNITIAIEKEECRFCISINTTWCAGYCYTRDLVYKDPARPKIQKTCTFKELVYET 78

Qy 177 VRVPGCAHHADSLYTPVATQCHCGKCDSDSTDCTVRGLGPSYCSFGEMKE 227

|||||  
Db 79 VRVPGCAHHADSLYTPVATQCHCGKCDSDSTDCTVRGLGPSYCSFGEMKE 129

It would have been obvious for one of ordinary skill in the art to use the method disclosed by Lustbader to construct a synthetic FSH chimeric polypeptide comprising an alpha-FSH subunit and beta-FSH subunits taught by Florkiewicz and Boime, with or without the half-life-increasing moiety as disclosed by Lustbader, to construct molecules with different half lives. One of ordinary skill in the art would have been motivated to construct such a polypeptide based on the teaching of Lustbader, which show that, the half life of

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FSH chimeric polypeptide can be increased or decreased depending on which life-increasing moiety is used. One of ordinary skill in the art would have had a reasonable expectation of success in constructing a chimeric polypeptide comprising an alpha-FSH subunit and a beta-FSH subunit because Lustbader routinely constructed similar types of molecules. Therefore, the claimed invention was obvious at the time of the invention.

7. No claim is allowed.



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Advisory

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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11/2/06



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